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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/690,495	10/21/2003	Arthur M. Krieg	C1039.70083US00	8657

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EXAMINER	
ARCHIE, NINA	

ART UNIT	PAPER NUMBER
1645	

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12/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/690,495	KRIEG ET AL.	
	Examiner	Art Unit	
	Nina A. Archie	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *52-77* is/are pending in the application.

4a) Of the above claim(s) *57 and 65-77* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *52-56 and 58-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :10/2/2007, 10/24/2007, 11/2/2007.

DETAILED ACTION

1. This Office Action is responsive to Applicant's amendment and response filed on 10-2-07. Claims 52-77 are pending. Claims 54, 60, and 64 are amended.

Information Disclosure Statement

2. The information disclosure statement filed on 10/2/2007, 10/24/2007, and 11/2/2007 has been considered. Initialed copies are enclosed.

Rejections Withdrawn

3. In view of the Applicant's amendment and remark following rejections are withdrawn.

a) Rejection to claim 54 under 35 U.S.C. 112, first paragraph, page 3 paragraphs 3-5, page 4 paragraph 1 is withdrawn in light of applicant's amendment thereto.

b) Rejection to claim 54 under 35 U.S.C. 112, first paragraph, pages 3-7 is withdrawn in light of applicant's amendment thereto.

c) Rejection to claim 60 under 35 U.S.C. 112, second paragraph, page 7 paragraph 2 is withdrawn in light of applicant's amendment thereto

Claim Objections/Rejections Maintained

Claim Objections

4. Claims 64 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter is maintained for the reasons set for in the previous office action.

Applicant arguments:

Claim 64 is objected to under 37 CFR 1.75(c) as being of improper dependent form. Applicant has amended claim 64 to recite that the composition is formulated for intravenous or intraperitoneal administration. Support for this amendment can be found on page 22, lines 9-15. Reconsideration and withdrawal of this objection is respectfully requested.

Examiner's Response to Applicant's Arguments:

Examiner accepts amendment to claim 64. However, the claim 64 is drawn to a composition and the route of administration has no patentable weight on the structure of the composition.

35 USC § 102 and 103

Claim Rejection - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

5. The rejection of claims 52-61, 63-64 are rejected under 35 U.S.C. 102(e) as being anticipated by Hutcherson et al US Patent 5,723,335 March 3, 1998 (filed March 25, 1994) is maintained for the reason set forth in the previous office action.

Applicant arguments:

Hutcherson et al. teaches that oligonucleotides having at least one phosphorothioate internucleotide linkage are immunostimulatory by virtue of this backbone modification. Hutcherson et al. does not teach that CG-containing oligonucleotides are immunostimulatory by virtue of the CG dinucleotide. Hutcherson et al. does not formulate any of these oligonucleotides with liposomes or cationic lipids. See for example col. 10 lines 14-16 which teaches that the buffer control contains sodium acetate and sodium chloride. Therefore Hutcherson et al. does not teach an immunostimulatory CpG containing oligonucleotide associated with a lipid or a sterol, and it therefore does not anticipate the rejected claims.

Examiner's Response to Applicant's Arguments:

The examiner disagrees with Applicant's assertion that Hutcherson et al. does not formulate any of these oligonucleotides with liposomes or cationic lipids. The claims are drawn to a composition for activating a non-specific immune response in a subject comprising: an oligonucleotide delivery complex, wherein the oligonucleotide delivery complex contains an immunostimulatory CpG containing oligonucleotide associated with a lipid, wherein the lipid is a liposome, wherein the composition activates a systemic, non-specific immune response in the subject.

Hutcherson et al teach a composition for activating a non-specific immune response in a subject (see column 5 lines 40-67, column 6 lines 31-43, column 7 lines 55-67, column 10 lines 46-57) comprising: an oligonucleotide delivery complex, wherein the oligonucleotide delivery complex contains an immunostimulatory CpG containing oligonucleotide (see SEQ ID NOs. 1, 2, 3) associated (i.e. formulated) with a lipid wherein the lipid is a liposome (column 8 lines 50-55). Hutcherson et al teach a composition, wherein the non-specific immune response comprises stimulating lymphocytes thus stimulating natural killer (NK) cell activity (see column lines 6 31-39, column 10 lines 58-67), wherein the CpG includes a phosphate backbone modification is a phosphorothioate (see abstract, column 5 lines 40-59, column 8 lines 31-50), wherein the oligonucleotide is 8-100 nucleotides in length (see SEQ ID NOs. 1, 2, 3). Therefore, Hutcherson et al meet the limitation of the instant claims.

As outlined previously, the instant claims are to drawn a composition for activating a non-specific immune response in a subject comprising: an oligonucleotide delivery complex, wherein the oligonucleotide delivery complex contains an immunostimulatory CpG containing oligonucleotide associated with a lipid, wherein the lipid is a liposome, wherein the composition activates a systemic, non-specific immune response in the subject.

Hutcherson et al teach a composition for activating a non-specific immune response in a subject (see column 5 lines 40-67, column 6 lines 31-43, column 7 lines 55-67, column 10 lines 46-57) comprising: an oligonucleotide delivery complex, wherein

the oligonucleotide delivery complex contains an immunostimulatory CpG containing oligonucleotide (see SEQ ID NOs. 1, 2, 3) associated with a lipid wherein the lipid is a liposome (column 8 lines 50-55). Hutcherson et al teach a composition, wherein the non-specific immune response comprises stimulating lymphocytes thus stimulating natural killer (NK) cell activity (see column lines 6 31-39, column 10 lines 58-67), wherein the CpG includes a phosphate backbone modification is a phosphorothioate (see abstract, column 5 lines 40-59, column 8 lines 31-50), wherein the oligonucleotide is 8-100 nucleotides in length (see SEQ ID NOs. 1, 2, 3), wherein the oligonucleotide comprises the formula 5' X1X2CGX3X4 3' wherein C and G are unmethylated, Xl, X2, X3 and X4 are nucleotides and a GCG trinucleotide sequence is not present at or near the 5' or 3' termini (see SEQ ID NOs. 1, 2, 3). Hutcherson et al teach a composition comprising a pharmaceutically acceptable carrier (see column 7 lines 49-55), wherein the oligonucleotide is synthetic (see column 8 lines 32-41).

Regarding the recitation of a composition for "activating a non-specific immune response" when administered by an intravenous or intraperitoneal route (claim 64); said recitation is considered an intended use and thus is given no patentable weight on the composition. Therefore the claims are drawn to a composition comprising an oligonucleotide delivery complex.

Claim Rejection - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. The rejection of claim 62 is rejected under 103(a) as being unpatentable over Hutcherson et al US Patent 5,723,335 March 3, 1998 (filed March 25, 1994) in view of Felgner et al US Patent 5,703,055 December 30, 1997 (filed January, 26, 1994) is maintained for the reason set forth in the previous office action.

Applicant arguments:

A prima facie case of obviousness has not been made because there is no motivation to combine the references, no reasonable expectation of success relating to such combination, and the combination does not yield every limitation of the pending claims.

Examiner's Response to Applicant's Arguments:

Examiner disagrees with Applicant's assertion that Hutcherson et al. does not teach that these oligonucleotides must contain a CG dinucleotide in order to be immunostimulatory. The claims are drawn to a composition for activating a non-specific immune response in a subject comprising: an oligonucleotide delivery complex, wherein the oligonucleotide delivery complex contains an immunostimulatory CpG containing oligonucleotide associated with a lipid, wherein the lipid is a liposome, wherein the

composition activates a systemic, non-specific immune response in the subject. Therefore Hutcherson et al meet the limitations of the claims. Examiner disagrees with Applicant's assertion that the combination of Hutcherson et al. and Felgner that does not yield each and every limitation of claim 62, as the combination does not lead one of ordinary skill in the art to an appreciation of the immunostimulatory capacity of a CG dinucleotide. There is motivation to combine Hutcherson et al. and Felgner. Hutcherson et al teach a composition for activating a non-specific immune response in a subject (see column 5 lines 40-67, column 6 lines 31-43, column 7 lines 55-67, column 10 lines 46-57) comprising: an oligonucleotide delivery complex, wherein the oligonucleotide delivery complex contains an immunostimulatory CpG containing oligonucleotide (see SEQ ID NOs. 1, 2, 3) associated with a lipid wherein the lipid is a liposome (column 8 lines 50-55). Hutcherson et al teach a composition, wherein the non-specific immune response comprises stimulating lymphocytes thus stimulating natural killer (NK) cell activity (see column lines 6 31-39, column 10 lines 58-67), wherein the CpG includes a phosphate backbone modification is a phosphorothioate (see abstract, column 5 lines 40-59, column 8 lines 31-50), wherein the oligonucleotide is 8-100 nucleotides in length (see SEQ ID NOs. 1, 2, 3). Felgner et al teach a composition wherein the oligonucleotide is encapsulated in the cationic liposome oligonucleotide (see abstract, column 8 lines 43-50, column 9 lines 24-31, column 22 lines 25-40, column 25 lines 63-65). Therefore one would have been motivated to encapsulate an oligonucleotide into cationic liposome taught by Felgner et al and that liposomes enhance the uptake of oligonucleotides taught by Hutcherson et al because Hutcherson et al and Felgner et al teaches a composition for activating a non-specific immune response comprising an oligonucleotide delivery complex.

As outlined previously, the instant claims are to drawn to a composition for activating a non-specific immune response in a subject comprising: an oligonucleotide delivery complex, wherein the oligonucleotide delivery complex contains an immunostimulatory CpG containing oligonucleotide associated with a lipid, wherein the

lipid is a liposome, wherein the composition activates a systemic, non-specific immune response in the subject.

Felgner et al teach a composition wherein the oligonucleotide is encapsulated in the cationic liposome oligonucleotide (see abstract, column 8 lines 43-50, column 9 lines 24-31, column 22 lines 25-40, column 25 lines 63-65). Felgner et al teach a composition comprising an oligonucleotide and a pharmaceutically acceptable carrier (see column 4 lines 65-67, column 5 lines 1-4).

It would have been prima facie obvious at the time the invention was made to encapsulate an oligonucleotide into cationic liposome taught by Felgner et al and that liposomes enhance the uptake of oligonucleotides taught by Hutcherson et al because Hutcherson et al and Felgner et al teaches a composition for activating a non-specific immune response comprising an oligonucleotide delivery complex.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 54 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim recites the phrase "wherein the CpG is not a part of a 6 base palindromic sequence". Although Applicant filed an explanation in the Applicants Arguments/Remarks on 10/2/2007 of a CpG that is not part of a 6 base palimdromic sequence, which activates a non-specific immune response in a subject. The conception of the new subgenus "not part of a 6 base palindrome sequence" is not conveyed in the specification (see pg. 13 lines 36-38) as outlined in the Applicants Arguments/Remarks on 10/2/2007. Therefore it is not clear if the claim or specification give the CpG that does not have part of a 6 base palimdromic sequence the function of activating a non-specific immune response in a subject. This is a new matter rejection.

Conclusion

Status of the Claims

8. Claims 52-64 are rejected.

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nina A Archie
Examiner
GAU 1645
REM 3B31

MARK NAVARRO
PRIMARY EXAMINER